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## TOPICAL AGENTS FOR BACTERIAL SKIN INFECTIONS

The large number of topical antibacterial agents offered for the treatment of skin infections is somewhat disproportionate to their usefulness; nevertheless, they are clearly valuable in impetigo and they are at times helpful in other primary and secondary infections, including those of the external ear canal.

ACUTE INFECTIONS - In the absence of a culture, the choice of an antibacterial agent for a superficial skin infection should be based on the fact that staphylococci are the usual invaders, with beta hemolytic streptococci usually appearing in the infected area after a few days (C. T. Nelson and J. T. McCarthy, Med. Clin. N. Amer., 43: 869, 1959). While neomycin is active against both organisms, it is much less effective than bacitracin against streptococci; therefore a mixture of these two antibiotics (500 units of bacitracin and 5 mg. of neomycin sulfate per gram (Bacimycin — Walker; Bacitracin-Neomycin Ointment — Rexall; and others) is usually the topical agent of first choice.

Tyrothricin, 0.5 mg. per gram (as in Tyroderm — Merck) and 1% erythromycin ointment (Erythrocin Ointment — Abbott; Ilotycin Ointment — Lilly) are also effective against staphylococcal and streptococcal skin infections, though they are unlikely to clear infections which are resistant to neomycin and bacitracin. Polymyxin B is somewhat more active than neomycin against Pseudomonas aeruginosa, a common invader in external otitis; for this infection, therefore, polymyxin B should be prescribed in combination with bacitracin-neomycin (Neo-Polycin Otic Ointment — Pitman, Moore; Neosporin Ointment — Burroughs Wellcome; and others).

CHRONIC INFECTIONS - In chronic superficial skin infections, which are usually secondary to a chronic dermatosis (such as eczema or seborrhea), both gram-positive and gram-negative flora may be present, and the bacitracin-neomycin combination or one of the topical broad-spectrum antibiotics (such as 3% tetracycline or 1% chloramphenicol) may be prescribed. The belief that systemic antiinfectives should not be used on the skin because of the risk of subsequent allergic reactions to the systemic preparation has been found valid so far only with penicillin and the sulfonamides. Some physicians nevertheless favor the broad-spectrum chemotherapeutic agents which are not used systemically, such as oxyquinoline compounds (Vioform — Ciba; Diodoquin — Searle; Sterosan — Geigy), or quaternary ammonium compounds such as triclobisonium (Triburon — Roche).

LIMITATIONS - Of the three primary skin infections (impetigo, ecthyma and folliculitis) for which topical antibacterial agents are commonly employed, impetigo is the most superficial and responds best to topical therapy. Impetigo, ecthyma and severe folliculitis or secondary skin infections are potential sites of staphylococcal and streptococcal invasion; if they do not improve with topical therapy in 48 hours (or if there is a history of nephritis, endocarditis or rheumatic fever), they should be treated systemically, preferably with oral penicillin. Topical antibacterial therapy has not been found useful for either prophylaxis or treatment of infections in wounds and burns. Eczematous and seborrheic lesions are often the sites of secondary infections, but little is gained from treating such lesions with topical antibacterials if the primary dermatoses are neglected (Nelson and McCarthy, cited above).

SENSITIZATION - All chemical antibacterial agents and some antibiotics occasionally cause sensitization. Topical penicillin and sulfonamide preparations are notorious in this respect, and their use is discouraged by practically all authorities; nevertheless, a number of penicillin and sulfonamide skin preparations are still being marketed. Nitrofurazone (Furacin — Eaton) is a potent sensitizer as well as a primary irritant, and Medical Letter consultants believe that its use in preference to other agents is never warranted. Next in order of sensitizing tendency are the oxyquinoline derivatives, quaternary ammonium compounds, and ammoniated mercury. Sensitization reactions occasionally occur after topical use of neomycin and other polypeptide antibiotics; such reactions are rare with topical tetracycline, erythromycin and chloramphenicol. Ammoniated mercury should not be applied to large areas of the body because of the risk of absorption.

RESISTANCE - The use of topical antibacterial agents seldom leads to the development or emergence of resistant strains of bacteria. These agents are applied to the skin in concentrations far in excess of those employed in systemic therapy, and usually for only a few days; therefore, strains of intermediate sensitivity have little opportunity to persist or to build up resistance. Cutaneous superinfections, particularly by monilia, have, however, been observed after topical application of broad-spectrum antibiotics (C. S. Livingood, et al., JAMA, 153:1266, 1953).

APPLICATION - For an antibacterial agent to be effective, it must come in physical contact with the bacteria. Therefore, it is important that crusts and scales be mechanically removed before the agent is applied. Dressings or soaks of warm saline solution are helpful in softening crusts. Unless there is much itching, eczematization or edema, the addition of a topical corticosteroid is not likely to be helpful. Where there is oozing pus, astringent compresses such as Burow's solution (1:20) should be used to minimize the oozing before a topical agent is applied.

Antibacterial agents are usually best employed in water-miscible cream or lotion form, though some are available only as ointments. Spray and aerosol preparations are sometimes more convenient, but there has not been sufficient experience with them to permit an appraisal of their effectiveness. Powdered forms of bacitracin, neomycin, Vioform and tetracycline are available for dusting on ulcerated lesions of the skin.

## ELAVIL

Amitriptyline hydrochloride (Elavil — Merck) is a cyclic dibenzyl compound closely resembling imipramine (Tofranil — Geigy) in structure and pharmacologic properties. According to the manufacturer, the drug is indicated in all depressions, and clinical studies are cited to show that "in frank depression, and in depression screened by anxiety and tension, Elavil has no equal."

Tofranil and to a lesser extent the monamine oxidase (MAO) inhibiting drugs have established their effectiveness in relieving severe depressive syndromes in many patients (Medical Letter, 3: 9, 1961). Contrary to the manufacturer's claims, Elavil has not been proved superior to Tofranil, nor has it been found useful in all depressions. Medical Letter consultants familiar with the drug believe, in fact, that it is quite similar to Tofranil in efficacy, speed of action, and range of usefulness. Despite reports indicating that its side effects are less severe than those of Tofranil and the MAO-inhibiting drugs, it is much too early to judge the toxicity of Elavil. Any potent new drug may after a time show unanticipated severe toxicity.

ACTIVITY - Like Tofranil, Elavil does not inhibit monamine oxidase, it has anticholinergic and antihistaminic properties, and in animal studies it shows sedative effects. These effects, together with the appearance of drowsiness in many patients, are responsible for the claim that the drug "has a tranquilizing component which makes it particularly useful in depressed patients in whom anxiety or agitation is a predominant symptom."

The claims for Elavil find support in papers included in the Symposium on Depression, Diseases of the Nervous System, Section 2, Supplement, May 1961, and in other reports listed in the manufacturer's brochure. But most of the studies were uncontrolled, and they generally fail to separate the effects of Elavil from those of other drugs used simultaneously, or to acknowledge the contribution to the reported improvement of psychotherapy or spontaneous remission. Even so, many of the writers — contrary to the manufacturer's claims — found the drug relatively ineffective in reactive depression and neurotic depression. This observation parallels the experience with Tofranil and the MAO inhibitors.

TOXICITY - The anticholinergic action of the drug has caused the most frequent symptoms, including dry mouth, blurred vision, tachycardia and urinary difficulties. The manufacturer warns against the use of Elavil in patients with glaucoma or urinary retention. To date there have been no reports of marked hypotension, cardiac complications, jaundice, or agranulocytosis, such as are occasionally noted with Tofranil; or of the hepatic damage sometimes associated with the use of MAO-inhibitors (C. D. Holdsworth, et al., Lancet, 2:621, Sept. 16, 1961). The manufacturer warns that "the schizophrenic symptomatology may be activated by Elavil" as it is by other potent antidepressant agents; the "tendency for antidepressant medication to provoke mania or hypomania in manic-depressive patients" is also noted. Elavil should not be employed along with other antidepressants, particularly the MAO-inhibiting drugs, because of the possibility of dangerous synergistic effects. As with Tofranil, the development of tolerance, euphoria, or addiction has not been reported.

DOSAGE - The initial dosage recommended by the manufacturer is 25 mg. three times a day. Dosages as high as 200 to 300 mg. have been given to hospitalized patients, but at this dose toxic reactions increase sharply without added benefits. If the response is favorable it generally becomes apparent in two to three weeks.

If preliminary observations are confirmed, Elavil will be a useful additional drug resource for the treatment of some psychotic depressions. There is no reason to believe that it will be effective where other drugs have shown little effect, that is, in depressions associated with organic brain disease, in the labile neurotic depressions, or in reactive depressions. For the suicidal depression, electroconvulsive therapy must still be considered the first choice; for the depression of involutional melancholia and manic-depressive psychoses, Tofranil or an MAO-inhibitor such as isocarboxazid (Marplan — Roche) or phenelzine (Nardil — Warner, Chilcott) is worth trying, and Elavil may after longer experience be added to this group; for moderate depressions such as occur with physical disease, post-viral states and psychoneuroses, dextroamphetamine rather than one of these newer drugs should be tried.

## NUTRAMENT

The commercial success of Metrecal (Mead Johnson) and other "900-calorie" liquid preparations for weight reduction has been followed by the marketing of Nutrament (Mead Johnson), a "nutritious meal, ready to drink," for normal persons who don't eat regular meals; for patients who cannot take solid food; and for the prevention and treatment of nutritional deficiencies. Each 12 1/2-fluid-ounce can of Nutrament liquid supplies 400 calories, of which 20 per cent or 20 grams is protein, 30 per cent fat (both derived from milk and soy flour), and 50 per cent carbohydrate. The formula also contains a variety of vitamins and minerals.

A person whose diet is generally unbalanced or otherwise inadequate can profitably substitute a can of Nutrament for a lunch consisting of pie and coffee or some other snack. But it is doubtful that he will enjoy it enough to continue the practice very long, and he should be encouraged to improve his diet rather than depend on Nutrament. Several persons who tried it complained of a chalky taste, medicinal after-taste, "synthetic" taste, etc.

HAM OR SWISS - A person on a generally adequate diet doesn't need Nutrament; he will do as well by lunching on a ham or Swiss cheese sandwich. (He won't get all the vitamins and minerals present in Nutrament; but there is no need for them at every meal.) Patients who for a time cannot consume solid foods because of oral, dental or surgical problems are likely to find other liquid foods more acceptable than Nutrament. Milk, milk shakes made with whole milk or skim-milk powder, egg nogs, and fluid emulsions of puréed meat and vegetable products can be used. Citrus juices can provide vitamin C. There appears to be no good reason for physicians to encourage the use of Nutrament.

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CORRECTION in the appraisal of vitamin K preparations (Medical Letter, 3:67, August 18, 1961): Lilly, not Abbott, manufactures Kappadione.

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